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# Does the scientific evidence support the advertising claims made for products containing *Lactobacillus casei* and *Bifidobacterium lactis*? A systematic review

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## ABSTRACT

**Background** To analyse the scientific evidence that exists for the advertising claims made for two products containing *Lactobacillus casei* and *Bifidobacterium lactis* and to conduct a comparison between the published literature and what is presented in the corporate website.

**Methods** Systematic review, using Medline through Pubmed and Embase. We included human clinical trials that exclusively measured the effect of *Lactobacillus casei* or *Bifidobacterium lactis* on a healthy population, and where the objective was related to the health claims made for certain products in advertising. We assessed the levels of evidence and the strength of the recommendation according to the classification criteria established by the Oxford Centre for Evidence Based Medicine (CEBM). We also assessed the outcomes of the studies published on the website that did not appear in the search.

**Results** Of the 440 articles identified, 16 met the inclusion criteria. Only four (25%) of these presented a level of evidence of 1b and a recommendation grade of A, all corresponding to studies on product containing *Bifidobacterium lactis*, and only 12 of the 16 studies were published on the corporate website (47%).

**Conclusions** There is insufficient scientific evidence to support the health claims made for these products, especially in the case of product containing *Lactobacillus casei*.

**Keywords** *Bifidobacterium*, fermented milk products, *Lactobacillus casei*, probiotics, systematic review

## Introduction

Functional foods were first developed in 1984 in Japan, in response to the widespread interest in improving health and reducing the risk of cardiovascular disease through diet.<sup>1</sup> Thought to have more beneficial health properties than conventional foods, functional foods have become a business opportunity for the food industry, which has invested millions of dollars in their development.<sup>2</sup> In the case of fermented milks and yogurt, these have been produced for centuries in the Mediterranean region, providing benefits in other areas such as body weight.<sup>3</sup>

This has been accompanied by strong marketing campaigns using various channels to promote their benefits through health claims made in advertising. The use of health claims is very similar to the approach used by medical corporations, which transmit seductive messages suggesting that ‘perfect

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health' can be achieved through the use of drugs.<sup>4,5</sup> This flood of probiotic products with supposedly beneficial and preventative properties also entails an increasing promotion of the ideology of health consciousness.<sup>6</sup>

105 Internationally, regulation of these foods is often unclear, creating an ambiguity which in practice results in lax controls. However, the USA and Japan have led the way in this respect, with legislation in place in both countries since 1990. They currently have two defined levels of required scientific rigour:  
 110 (i) high level of scientific evidence, known as 'significant scientific agreement' (SSA) in the USA and 'Foods for Specified Health Use' (FOSHU) in Japan, and (ii) low level of scientific evidence, known as 'qualified health claims' in the USA and 'qualified FOSHU' in Japan. The European Union only has a requirement  
 115 for a high level of scientific evidence, through Regulation 1924/2006 (sections 13 and 14),<sup>7</sup> issued relatively recently, in 2006.<sup>8</sup> Thus, the validity of health claims must be demonstrated to the European Food Safety Agency (EFSA)<sup>9</sup> in a report presenting the scientific evidence for the supposed beneficial effects that  
 120 consumption of the product has on health.

Despite the fact that the EFSA only takes a high level of scientific evidence into account, unlike its counterparts in the USA and Japan which also consider a lower level of evidence, and although studies measuring observance of existing legislation on nutrition and health claims are scarce, it would nevertheless appear that there is some degree of non-compliance on the part of food companies in this regard. Failure to meet the requirements of the Regulation as regards certain types of  
 125 health claims, the regular occurrence of unauthorized health claims and the less healthy nutritional profile of most products for which nutritional and/or health claims are made, may be creating a climate of confusion and could be misleading consumers.<sup>10</sup>

A widely cited example is the case of product containing  
 135 *Lactobacillus casei* and its associated controversial advertising campaigns.<sup>11</sup> In 2009, the Advertising Standards Authority (ASA) in the UK investigated a complaint lodged by a consumer about an advertisement in which the following message appeared: 'scientifically proven to help support your kid's defences', and ruled that the advertising claim was misleading and not supported by the studies presented, calling the French multinational to task and ordering them to withdraw the advertisement until it had been amended.<sup>12</sup> Danone has used a similar approach to promoting Actimel® as that used for other probiotics: advertisements that  
 140 depict the daily life of potential consumers, presenting the consumption of a probiotic product as a dietary habit and proclaiming its alleged health benefits.<sup>13</sup>

In accordance with Article 13.5 of the EU Regulation, which regulates claims supported by new scientific evidence  
 150 and/or that include an application for the protection of data

subject to intellectual property rights, the EFSA evaluates applications on a case-by-case basis. Specifically as regards the brands Actimel and Activia, the regulatory body has ruled that the following claims be 'withdrawn': (i) A fermented milk that contains the probiotic *Lactobacillus casei* DN 114001/CNCM I-1518 Actimel® and helps to maintain [contributes to] the intestinal defence function; (ii) A fermented milk that includes *Bifidobacterium lactis* DN-173 010/CNCM I-2494 and lactic acid bacteria Activia®, and improves gastrointestinal comfort; (iii) Activia® improves slow transit; (iv) Actimel® helps to strengthen the body's natural defences; (v) Activia® products are fermented milks that improve digestive comfort.

With respect to Article 14, on reducing a risk factor in the development of a disease, EFSA members considered that there was an insufficient cause–effect relationship between consumption of this product and disease reduction to support the following claim: Fermented milk that contains the probiotic *L. casei* DN 114001/CNCM I-1518 Actimel® and reduces the presence of *Clostridium difficile* toxins in the gut, associated with the incidence of acute diarrhoea. Consequently, this claim cannot be used in advertising, either.<sup>14</sup>

At present, April 2013, advertising for the product presents the following argument 'Actimel® contains *L. casei* Danone, Vitamin B6 and D, which support the normal function of the immune system' and 'Actimel® contains the exclusive *L. casei* Danone and Vitamin B6 to support the immune system and reduce fatigue'. As can be seen, the product is enriched with vitamins B6 and D. According to Regulation (EC) no. 432/2012, which establishes a list of permitted health claims for foods other than those related to disease risk reduction and child development and health, vitamin B6 'helps reduce tiredness and fatigue' and—together with vitamin D—'contributes to the normal function of the immune system', among other properties. Thus, the health-related arguments presented in the product advertising are in line with current legislation.

Studies have been conducted on the public's attitude to the consumption of probiotics. Brands such as Actimel®, Yakult® and Benecol® are the first to be named. When exploring public perceptions of probiotics, consumers reported scientific uncertainty and personal fears, indicating that purchasing decisions are heavily influenced by the beliefs and feelings generated by advertising. Also of concern is the possibility that the advertising of these products and their consumption may produce health side effects.<sup>15</sup> One example of this is the feeling of being a 'good mother' that women report experiencing when they purchase probiotic foods for their families.<sup>16</sup>

The company has a large presence in the field of nutrition through the Danone Institute, which fosters and disseminates scientific information that is subsequently used in advertising,

alluding to the supposedly benefits. This aspect is of considerable importance, given the controversy elicited to date by industry-funded science.<sup>17</sup>

Danone's health claims are that product containing *L. casei* strengthens the body's natural defences, and product containing *B. lactis* improves intestinal transit. To clarify the scientific evidence supporting its advertising claims and to conduct a comparison between the published literature and that presented on the company's website,<sup>18</sup> this paper reports a systematic analysis of the studies that refer to the strains contained in the products promoted on the Danone website. More specifically, the aim of this study was to:

- (a) determine the scientific evidence presented in studies to support the health claims.
- (b) compare the studies identified in a literature search with those presented by Danone on its website and identify any bias in the information provided.

## Methods

### Literature search profile

A literature search was conducted in Medline via Pubmed and Embase between September and October, 2012. Previously searched the Danone corporate website to identify all studies published there on the products containing *L. casei* and *B. lactis*. Terms were selected following a review of those used in the studies published on Danone's corporate website. The terms chosen were: 'fermented milk product', '*Lactobacillus casei*' and '*Bifidobacterium*'. The search equation was: ([MeSH Term] Fermented milk product) AND (([MeSH Term] *Lactobacillus casei*) OR ([MeSH Term] *Bifidobacterium*)).

### Inclusion and exclusion criteria

We included studies on human clinical trials, published in English and Spanish, in which only the effect of the milk product on a healthy population was measured, and where the objective was related to the health claims made for the product in advertising: improving defences (product containing *L. casei*) and improved intestinal transit (product containing *B. lactis*).

We excluded studies that did not meet the above criteria, consisting of research measuring the effect of the milk product in conjunction with a medication or other component, studies on populations with pathologies, studies that used other probiotic strains, studies using a different form of administration to the format studied (capsules, milk products for reconstitution, cheese, cereals) and studies that measured other effects unrelated to the health claims made for the products.

Although one of the inclusion criteria was that the studies should have been conducted on healthy subjects, it was

decided to include two studies<sup>19,20</sup> on people with irritable bowel syndrome, since the advertising for the product that containing *B. lactis* claims that it improves the symptoms of this disease.

### Analysis of the scientific literature

Information on the following variables was extracted from the studies finally selected for the systematic review: authors, journal name, year of publication, sample size, design, country of origin of the study, outcomes, key findings and source of funding for the study. We assessed the levels of evidence and strength of recommendation according to the classification criteria established by the Oxford Centre for Evidence Based Medicine (CEBM).<sup>21</sup> Levels were classified from 1 to 5, where Level 1a corresponded to the maximum recommendation Grade A and Level 5 corresponded to Grade D, where the recommendation was neither endorsed nor rejected. We also evaluated the outcomes of the studies published on the website which did not meet the inclusion criteria.

To help assess the quality of each article, reviewers used CONSORT checklists. From a total of 25 topics per checklist, each article received a score of 1 point if the publication met the criteria and 0 point if it did not. For the quality of the articles included, see Tables 1 and 2.

## Results

The initial search identified 440 articles: 395 articles in Pubmed and 149 in Embase, of which 104 were duplicates, leaving 45 additional articles in Embase. Following an initial review, 420 articles were excluded, consisting of studies that measured the effect of the milk product in conjunction with a medication or other component ( $n = 34$ , 8.1%), studies on populations with pathologies ( $n = 152$ , 36.2%), studies using other probiotic strains ( $n = 81$ , 19.3%), studies using a different form of administration to the format studied ( $n = 63$ , 15%) and studies that measured other effects unrelated to the health claims made for the products ( $n = 90$ , 21.4%) (Fig. 1).

We selected 16 studies that met the inclusion criteria, the earliest of which was from 2001<sup>35</sup> and the most recent from 2011.<sup>29</sup> Two of these had been conducted on children<sup>26,29</sup> while the rest involved adults. Seven studies were conducted exclusively on women, one on men and eight on both sexes. Three of the studies were performed in Asia<sup>25,27,32</sup> and the remaining 13 in Europe. One study was written in Spanish<sup>26</sup> and the rest ( $n = 15$ ) in English. The design of the 16 studies are randomized controlled trials (RCT).

An analysis of the search results revealed that 12 of the 16 studies were cited on the corporate website. Thus, of the

**Table 1** Characteristics, results and limitations of the studies analysed on the effect of *Lactobacillus casei* in healthy populations

Authors	Study design	Sample size	Consort score	Age (sex)	Outcomes	Results	Limitations
Fabian <i>et al.</i> <sup>22</sup>	RCT	33	9	22–29 years old. (Females)	Plasma and urinary concentration of thiamine (B1), riboflavin (B2) and pyridoxine (B6)	No significant differences were found between the two groups; the results indicated that daily consumption of 200 g of both yoghourts (probiotic and conventional) for 2 weeks may contribute to levels of thiamine and riboflavin.	No limitations reported.
Ortiz-Andrellucchi <i>et al.</i> <sup>23</sup>	RCT	104	20	18–40 years old. (Females)	Analysis of immune system biomarkers (Th1/Th2, IgA, IgG, IgE, IgM, leukocytes, IL-4)	No significant differences observed between the treatment group and the control group for most of the biomarkers analysed.	Relative absence of functional analyses of T, NK and B cells.
Meyer <i>et al.</i> <sup>24</sup>	RCT	33	15	22–29 years old (Females)	Cytokine production	No significant differences observed in cytokine production between the group consuming conventional yoghourt and the group consuming yoghourt containing <i>L. casei</i> .	Several subjects were lost in follow-up. Failure to include a control group that did not consume yoghourt.
Takeda and Okumura <sup>25</sup>	RCT	19	6	30–75 years old. (Males and females)	NK cell activity	NK cell activity was significantly increased at Week 1 ( $P = 0.0598$ ) and Week 3 ( $P = 0.0050$ ) following the start of fermented milk intake, compared with NK cell activity at baseline.	No limitations reported.
Tormo Carnicer <i>et al.</i> <sup>26</sup>	RCT	35	15	1–3 years old. (Males and females)	Levels of immunoglobulin A (IgA) secreted in saliva when fed fermented milk with <i>L. casei</i> and <i>Streptococcus thermophilus</i>	The group of children fed fermented milk with <i>L. casei</i> demonstrated a significant increase ( $P = 0.0063$ ) in IgA levels secreted after 6 weeks of ingestion.	No limitations reported.
Morimoto <i>et al.</i> <sup>27</sup>	RCT	38	16	20–60 years old. (Males)	Relationship between smoking and NK cell activity. NK cell activity following consumption of fermented milk containing <i>L. casei</i>	No change found in the relative proportion of NK cells due to drinking fermented milk containing <i>L. casei</i> .	No limitations reported.
Marcos <i>et al.</i> <sup>28</sup>	RCT	155	12	18–23 years old. (Males and females)	Immunological measurements (number of lymphocytes, cytokine production, immunoglobulin)	The treatment had a significant effect in absolute terms on lymphocyte count after 6 weeks.	It is possible that the immunomodulatory action of lactic acid bacteria on lymphocyte count-influenced the CNS through modifications in cytokine balance.

**Table 2** Characteristics, results and limitations of the studies analysed on the effect of *Bifidobacterium lactis* in healthy populations

Authors	Study design	Sample size	Consort score	Age (sex)	Outcomes	Results	Limitations
Tabbers <i>et al.</i> <sup>29</sup>	RCT	202	23	18–60 years old. (Males and females)	Gastrointestinal well-being. Frequency of gastrointestinal symptoms. Frequency and consistency of stools	Stool frequency did not differ between the group consuming fermented milk products and the control group. A significant difference was found in self-reported gastrointestinal well-being and symptoms.	Possible laxative effect of the control product and possible loss effect in follow-up, although this percentage was similar in both groups.
Guyonnet <i>et al.</i> <sup>30</sup>	RCT	160	21	3–16 years old. (Males and females)	Frequency of bowel movements. Stool consistency	No significant difference found as regards increased stools between the group consuming the fermented milk product containing the <i>B. lactis</i> DN-173 010 strain group and the control group.	Limitation reported on data interpretation due to the use of multiple statistical comparisons.
Guyonnet <i>et al.</i> <sup>31</sup>	RCT	360	22	18–65 years old. (Males and females)	Gastrointestinal well-being. Self-report questionnaires measuring constipation, diarrhoea, stomach pain and gastrointestinal comfort	No significant difference observed in symptoms such as constipation, diarrhoea or stomach pain between the two groups receiving fermented milk and the control group. A higher percentage of the treated group were observed to report gastrointestinal comfort than the control group.	The percentage of participants reporting an improvement may be an overestimation, and it should be noted that not all items showed an improvement. Publicity may influence participants' expectations about the product.
Yang <i>et al.</i> <sup>32</sup>	RCT	135	18	25–65 years old (Females)	Frequency of bowel movements and stool consistency	Frequency of bowel movements increased significantly after 2 weeks of consumption ( $2.6 \pm 1.0$ versus $2.4 \pm 0.6$ , $P < 0.05$ ), but no differences were found after 1 week.	No limitations reported.
Agrawal <i>et al.</i> <sup>19</sup>	RCT	41	24	20–69 years old. (Females)	Symptoms of irritable bowel syndrome, bloating and intestinal transit	Intestinal transit time was significantly reduced.	Lack of objective measures of results since most of the symptoms, such as abdominal pain and bloating are completely dependent on patient self-reports.
Guyonnet <i>et al.</i> <sup>20</sup>	RCT	276	22	18–65 years old (Males and females)	Frequency of bowel movements and IBS symptoms	No significant differences found in frequency of bowel movements or stool consistency. An improvement was observed, however, in symptoms.	The high placebo effect may be due in part to advertising (TV, magazines, posters) health claims made for fermented milk products, such as those examined in the present study.
Meance <i>et al.</i> <sup>33</sup>	RCT	159	16	50–75 years old (Males and females)	Intestinal transit time	Significant differences found in intestinal transit following consumption of the probiotic milk product.	One limitation of this study was the possible psychological effect on transit time of subjects' awareness that they were consuming a potentially effective product.

*Continued*

Table 2 Continued

Authors	Study design	Sample size	Consort score	Age (sex)	Outcomes	Results	Limitations
Marteau <i>et al.</i> <sup>34</sup>	RCT	32	18	18–45 years old (Females)	Intestinal transit time and faecal bacterial mass	No significant differences found in intestinal transit time. However, a significant increase was observed in faecal bacterial mass during consumption of the fermented milk product.	It is possible that some effects of probiotics on colon bacteria may occur slowly and persist for > 10 days, which could be a limitation of the study.
Meance <i>et al.</i> <sup>35</sup>	RCT	90	14	60–75 years old (Males and females)	Intestinal transit time	Significant differences found in intestinal transit following consumption of the probiotic milk product.	No limitations reported.

47 articles available on the website, only 12 met the established inclusion criteria, and only 7 of those demonstrated some positive effect following consumption of milk products enriched with probiotic strains (Tables 1 and 2). The results for these seven articles showed that three of them concerning the *L. casei* strain<sup>25,26,28</sup> ( $n = 3$ , 19%) corresponded to Level 5 and recommendation Grade D, because they were based on circumstantial evidence and opinion, and none showed clinical effects in support of the health claims made, but rather reported effects on laboratory parameters.

In the case of the *B. lactis* strain<sup>19,32,33,35</sup> ( $n = 4$ , 25%), all four studies provided evidence corresponding to Level 1b and recommendation Grade A. For the remainder of the studies ( $n = 9$ , 56%), the results showed no differences, i.e. only four studies provided valid scientific evidence and all corresponded to *B. lactis*. The effect demonstrated in these four studies was decreased intestinal transit time. Two of the studies used male and female subjects,<sup>33,35</sup> and two were performed exclusively on females<sup>19,32</sup>

Another aspect analysed was the source of funding for these studies and the relationship with the company. Company funding was declared in 7 (44%) of the 16 studies. Two (12.5%) stated that the company had supplied the probiotic, another two (12.5%) reported that the company had supplied the probiotic and at least one of the authors appeared to be linked to the company, four (25%) did not mention funding nor product contribution but one of the authors appeared to be linked to the company and only one study (6%) did not mention funding from the company nor were any of the authors linked to the company.

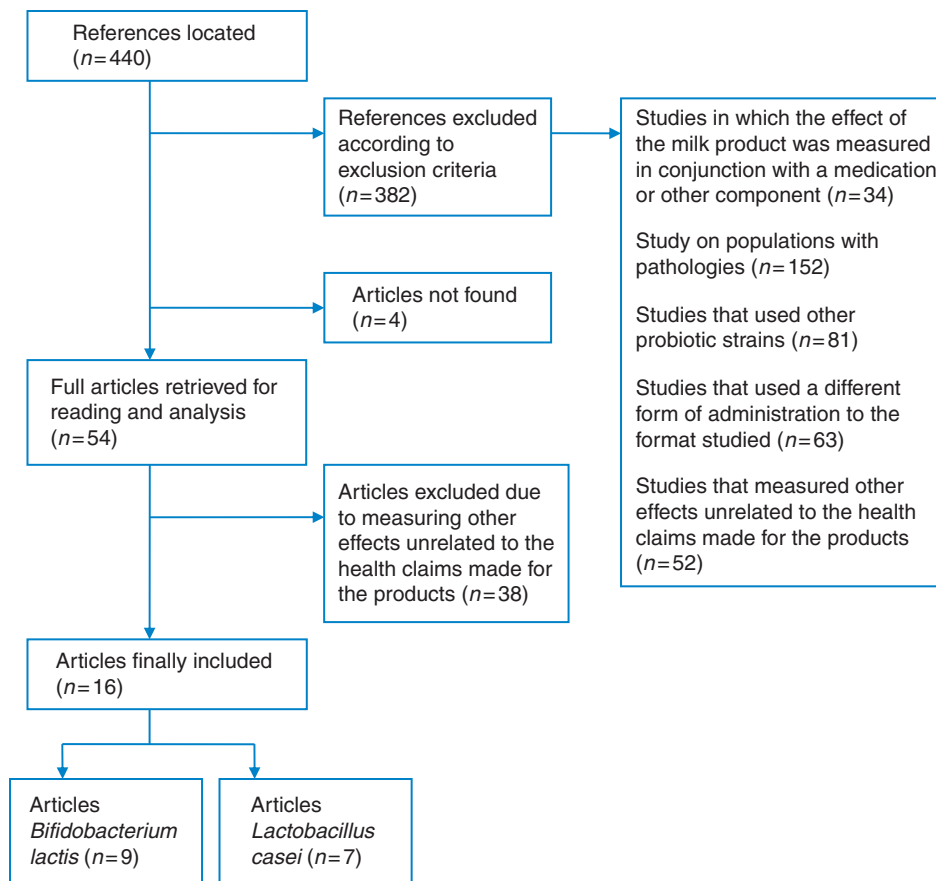
Lastly, we assessed the 35 studies published on the website that did not meet the inclusion criteria. Of these, 1 (2.9%) corresponded to a study on animals, 13 (37.1%) to studies on populations with pathologies, 18 (51.4%) to studies measuring effects other than those stated in health claims and 3 (8.6%) measured the effect of milk product consumption on a laboratory parameter.

Discussion

Main finding of this study

Our study reveals the limited scientific evidence in support of the health benefits attributed to these products in advertising and marketing. The evidence for *L. casei* is null, while only four studies support the health claims made for *B. lactis*. We conclude that the company’s advertisements for its products are biased, employing health claims that are not supported by sufficient scientific evidence based in these ingredients. Furthermore, the scientific material published on their corporate website is not related to the health claims used to advertise the milk products,





**Fig. 1** Diagram of the systematic review process.

and consumers may be confound into believing that it constitutes sufficient evidence for the consumption of these widely sold and advertised products, which could generate side effects. These results strongly suggest the need for new legislation on health claims made for food products, which as a minimum should prevent conflicts of interest.

The small number of articles found, which met the inclusion criteria and were also published on the company's website (12 of the 47 articles published on the website), could be a reflection of the diversity of objectives reported in studies on the website, i.e. mainly studies testing the effect of probiotic strains on specific pathologies or studies measuring an aspect unrelated to the health claims made for the product in question.

### What is already known on this topic

The strong presence and position in the market of these products, due, among other factors, to their advertising, renders this information of particular importance. The health claims used in this advertising are based on studies conducted by the company. However, as our study reveals, there is a worrying paucity of scientific evidence for these claims, leading to the conclusion that there is an information gap between the

advertising message and the expectations it fosters in potential consumers. Thus arises the controversial subject of 'nutritional altruism', whereby consumers feel good about buying these products for their families as a result of the health claims made in advertising, which are not always supported by sound scientific evidence.<sup>16</sup>

The results of a recent study analysing current regulations in the European Union and the USA are consistent with the findings reported here, namely that probiotic product advertising includes claims that the consumption of these products can confer health benefits. Although some of these claims may be valid, many have not been substantiated: the claims made for some products are based on insufficient research or weak studies. Nevertheless, consumers report that the product is good for them.<sup>36</sup>

### What this study adds

The lack of a clear definition of probiotics in the present regulatory framework, and the ease with which these can be placed on the market, yielding enormous economic benefits to companies with minimal investment in research, highlights the importance of formulating clear international standards



and the need for more rigorous and high-quality research.<sup>37</sup> The messages and arguments given today in much food advertising actually require much more quality scientific evidence to support the use of such health claims.

The aim of our study was to contribute to the scant available evidence on the subject and encourage the industry to give real importance to the use of health claims with good-quality scientific evidence to deliver clear messages to the public. We believe that companies have the necessary tools to accomplish this and hope that this situation will improve in the near future.

### Limitations of this study

In the present study, our analysis was limited to those studies in which there was a relationship between the objective and the health claim made for the product in question; this approach has enabled us to analyse the supposed efficacy of the milk product in a specific context and to determine consumers' expectations of these products at the time of purchase.

We have analysed the studies of the corporate website of one of the most important companies; however, there are other companies that also advertise products containing these substances. Future studies should look at advertising on the website of these companies.

It is also possible that the literature search conducted in this study was biased due to the exclusive inclusion of articles published in journals indexed by PubMed and Embase. However, the scientific literature recommends the use of these two databases for literature searches.<sup>38</sup>

### Conclusions

The fact that such an important multinational company uses health claims based on insufficient supporting scientific evidence should be borne in mind by policymakers and the competent authorities, who should amend the pertinent regulations to achieve higher standards as regards greater transparency in the food industry. Health professionals should also be aware of the magnitude of the health claims made by the food industry in advertising. This is important when recommending this type of food or warning about possible risks, e.g. the excessive use made of them or their use as a replacement for medication prescribed by a professional, due to the huge trust consumers place in advertising messages that can cause confusion or, worse, be misleading.

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